Remarks/Arguments

1. Confirmation of Allowable Subject Matter

According to the Office Action Summary, all the pending claims have been rejected. However, no rejections were set forth against claims 140, 149, 161 and 162. Therefore, it appears that these claims would be allowable but for their dependence on a rejected base claim. Confirmation of the allowable subject matter is respectfully requested.[1]

2. Priority Determination

According to the Office Action at pages 2 and 4, the priority date granted for claims 107-136 and 150-155 is 06/25/2005, whereas page 5 of the Office Action indicates that the priority date is 06/24/2005. Applicants presume that the priority date asserted for these claims is 06/24/2005 (the date the Preliminary Amendment was filed). The priority date granted for claims 137-168 and 170-173 is 04/19/2000 (the filing date of the parent PCT application). Applicants respectfully disagree with the priority determination.

At the outset, it is unclear how the priority date for claims 150-155 can be both 06/24/2005 and 04/19/2000. Clarification is requested.

It appears that the Examiner is trying to make a distinction with regard to the multitarget partially double stranded RNA and expression vectors encoding two or more RNA molecules in terms of priority. However, the parameters used to separate the priority dates are unclear. For instance, according to the Office Action at page 3, lines 10-13, the Examiner denies priority for claims 107-136 and 150-155 to the parent provisional and PCT applications because

the parent applications allegedly fail to disclose an expression vector comprising two or more promoters capable of expressing two or more double stranded RNA. Yet, according to the Action at page 3, lines 18-20, priority was denied only to the parent provisional application for claims 137-168 and 170-173 because the provisional application allegedly fails to contemplate an expression vector encoding two or more different double stranded RNA molecules. It appears that the Examiner uses the same reason for denying priority to both sets of claims, but comes out with a different result. Clarification is requested.

Similarly, claim 107 is directed to a multitarget partially double stranded RNA molecule comprising two or more different double stranded RNA sequences. Claim 141 is directed to an expression vector encoding a multitarget partially double stranded RNA molecule comprising two or more different double stranded RNA sequences. Yet the priority date granted to claim 107 is 06/24/2005, whereas the priority date granted to claim 141 is 04/19/2000. It is unclear how a vector encoding a multitarget partially double stranded RNA molecule comprising two or more different double stranded RNA sequences would have a different priority determination than the encoded multitarget RNA. Clarification is requested.

Further, the Examiner appears to be requiring that Applicants' priority applications disclose the claimed invention *in haec verba*, which is clearly improper. For instance, according to the Office Action at page 3, lines 7-10, the Examiner acknowledges that the provisional and PCT applications "disclose an expression vector capable of expressing two or more double stranded RNA molecules." However, in the next sentence, at page 3, lines 10-13, the Examiner denies priority for claims 107-136 and 150-155 to the parent

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[1] We may want to submit new independent claims based on claims 140, 149, 161 and 162.

provisional and PCT applications because the parent applications allegedly fail to disclose "an expression vector comprising two or more promoters capable of expressing two or more double stranded RNA." The skilled artisan reading the specification would clearly understand that one way to generate an expression vector capable of expressing two or more double stranded molecules would be to use two or more promoters, each expressing a double stranded molecule. The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. See MPEP 2163.02.

As noted above, the priority date granted for claims 107-136 and 150-155 is 06/24/2005 (the date the Preliminary Amendment was filed), because the Examiner believes that these claims are not supported by the instant as-filed specification. Support for claims 107-136 and 150-155 in the subject application is discussed below in response to the written description rejection. Since the present application is a national stage filing under 371, the PCT application has the same disclosure as the subject application. Accordingly, the response to the written description rejection below is equally applicable to the priority determination for these claims based on the parent PCT application, and Applicants respectfully submit that claims 107-136 and 150-155 should have benefit of priority, at the very least, to the PCT application.

Applicants further submit that the subject matter of at least claims 107-136 is disclosed in the parent provisional application 60/130,377. For example, at page 3, lines 7-24, the provisional specification discloses a composition comprising an at least partially double stranded RNA molecule that is substantially homologous to a target polynucleotide, and discloses that the RNA molecule may be produced recombinantly. At page 9, lines 7-8, the

provisional specification discloses that the double stranded portions of the molecules can occur at either or both termini. A partially double stranded molecule with double stranded portions at both termini implicitly contains at least two different double stranded regions. At page 10, lines 24-26, the provisional specification discloses that the molecules of the invention contain at least one segment of 30 contiguous nucleotides with homology to the target sequence. A partially double stranded molecule containing at least one segment having homology to a target sequence implicitly contains one or more different double stranded regions. Accordingly, claims 107-136 deserve the benefit of the provisional application filing date, which was 04/21/1999.

In view of all the remarks above, reconsideration and clarification of the priority determination is respectfully requested.

3. New Matter Rejection under 35 U.S.C. §112, First Paragraph

Claims 107-136 and 150-155 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. According to the Office Action (pp. 4-5), this is a "new matter rejection" and therefore, the effective filing date of claims 107-136 and 150-155 is considered to be 06/24/2005, which was the filing date of the amended claims.

At the outset, Applicants respectfully note that this is not an appropriate new matter rejection. According to MPEP 2163.01:

> If the examiner concludes that the claimed subject matter is not supported in an application as filed, this would result in a rejection of the claim on the ground of a lack of written description under 35 U.S.C. 112, first paragraph or denial of the benefit of the filing date of a previously filed application. The claim should not be rejected or objected to on the ground of new matter. As framed by the court in *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981), the concept of new matter is

> only properly employed as a basis for objection to amendments to the abstract, specification or drawings attempting to add new disclosure to that originally presented. (With emphasis.)

Turning now to the substance of the rejection, the Examiner acknowledges at page 4, last paragraph of the Office Action, that the specification discloses on page 8 a polynucleotide comprising an RNA that is targeted to one or more genes, and that the molecules of the invention are partially double stranded. However, the Examiner questions support for a multitarget partially double stranded RNA molecule comprising "two or more *different* double stranded RNA sequences" as recited in claim 107. Applicants respectfully traverse this ground for the rejection.

As stated on page 8, lines 19-20, of the specification, "the polynucleotide sequences described herein may employ a multitarget or polyepitope approach, *e.g.*, encoding sequences of more than one gene of a single target pathogen or against more than one target pathogen, or other category of target desired to be silenced" (with emphasis). This passage clearly implies that different target genes may be silenced using a single construct of the invention.

Further, it is clear from the disclosure that it is the double stranded sequences of the RNA molecules of the invention that have homology to the target gene. For instance, as disclosed on page 37, lines 1-6, double stranded RNA is expected to inhibit the synthesis of the target gene, whereas control sense and antisense molecules are expected to have only a modest, if any, inhibitory effect. See also page 20, lines 18-19, which specifies that the dsRNA is both homologous and complementary to the target sequence.

Given that it is clear from the disclosure that the double stranded regions of the partially double stranded molecules of the invention correspond to the target gene, and given that the specification discloses that the molecules of the invention may target more than one pathogen gene sequence, it would be clear to the skilled artisan reading the specification that multitarget partially double stranded RNA molecules comprising two or more different double stranded RNA sequences are disclosed. Reconsideration and withdrawal of this ground for the rejection are respectfully requested.

The Office Action further asserts, presumably with reference to claims 150-155, that the specification does not contemplate an expression vector comprising two or more promoters capable of expressing two or more double stranded RNAs (p. 5 of Office Action). Applicants respectfully traverse this ground for the rejection.

As stated on page 20, lines 17-19 of the specification, the vectors of the invention may be "designed to generate two or more, including a number of different dsRNAs homologous and complementary to a target sequence" (with emphasis). As stated on page 19, lines 18-21, the vectors of the invention are "designed to contain one of the promoters or multiple promoters in combination" (with emphasis). The skilled artisan reading these passages of the specification would clearly see that Applicants were in possession of an expression vector capable of expressing two or more double stranded molecules using two or more promoters, each expressing a double stranded molecule. The subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to

satisfy the description requirement. See MPEP 2163.02. To satisfy the written description requirement, a patent specification must only describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, *e.g.*, *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. Reconsideration and withdrawal of this ground for the rejection are respectfully requested.

In view of the above remarks, Applicants respectfully submit that claims 107-136 and 150-155 are adequately described in the instant specification. Since the present application is a national stage filing under 371, the PCT application has the same disclosure as the subject application. Accordingly, the response to the written description rejection below is equally applicable to the priority determination for these claims based on the parent PCT application, and Applicants respectfully submit that claims 107-136 and 150-155 should have benefit of priority, at the very least, to the parent PCT application.

4. Prior Art Rejections under 35 U.S.C. §102

Claims 107-108, 113-119, 121, 123, 125, 127-138, 141-148, 156-159, 163, 165, 167, 168 and 170-172 have been rejected under 35 U.S.C. §102(b) as being anticipated by Taira *et al.* (US 5,500,357) (hereinafter US '357). According to the Office Action, US '357 teaches a multitarget partially double stranded RNA molecule comprising two or more different double stranded RNA sequences that are substantially homologous and

complementary to two or more sequences of a target gene (with reference to Figure 3). Applicants respectfully traverse the rejection.

US '357 teaches transacting ribozymes flanked by 5' and 3' cis-acting ribozymes, which may be connected in tandem (col. 6, lines 65-67). With reference to Figure 3, the reference teaches that multiple ribozymes may be expressed as a single RNA molecule where all the ribozymes are connected in tandem, and may be trimmed at the 5' and 3' ends of each ribozyme by the action of the cis-acting ribozymes following transcription. At no point does US '357 teach a multitarget partially double stranded RNA molecule comprising two or more different double stranded RNA sequences that are substantially homologous and complementary to two or more sequences of a target gene, as recited in claim 107.

As depicted in Figure 1 of US '357, ribozymes do contain sequences that are complementary to the target gene (segment C in Figure 1). Further, ribozymes do contain a partially double stranded catalytic segment (segment B in Figure 1). However, the double stranded segment in a ribozyme is neither homologous nor complementary to the target gene. Accordingly, US '357 does not anticipate claim 107. Claims 108, 113-119, 121, 123, 125 and 127-136 are dependent directly or indirectly on claim 107 and therefore incorporate all the limitations thereof. Accordingly, US '357 also fails to anticipate these dependent claims.

Similarly, claim 137 is directed to an expression vector encoding two or more different double stranded RNA sequences that are homologous and complementary to two or more sequences of at least one target gene. As explained above, US '357

concerns ribozymes and therefore does not teach the expression of double stranded RNA sequences that are homologous and complementary to a target gene. Claims 138, 141-148, 156-159, 163, 165, 167, 168 and 170-172 are dependent directly or indirectly on claim 137 and therefore incorporate all the limitations thereof. Accordingly, US '357 also fails to anticipate these dependent claims.

In view of the above remarks, reconsideration and withdrawal of the rejection under §102(b) based on US '357 are respectfully requested.

Claims 107, 109, 111-117, 119, 121, 123-137, 139, 141-148, 156-157, 159, 163, 165, 167, 168 and 170-173 have been rejected under 35 U.S.C. §102(b) as being anticipated by Chen *et al.* (Nucleic Acids Res. 1992) (hereinafter Chen). According to the Office Action, Chen teaches a multitarget partially double stranded RNA molecule comprising from 2 to 9 different double stranded RNA sequences that are substantially homologous and complementary to two or more sequences of an HIV target gene (with reference to Figure 2). Applicants respectfully traverse the rejection.

Like US '357, discussed above, Chen discloses multitarget ribozymes. As depicted in Figure 2 of Chen, ribozymes contain sequences that are complementary to the target gene (which, in the case of Figure 2, is the HIV-1 env gene). Further, ribozymes do contain a partially double stranded catalytic segment (the Hammerhead Rz37 region shown in Figure 2). However, the double stranded segment in the ribozyme is neither homologous nor complementary to the target gene. Accordingly, Chen does not anticipate claim 107. Claims 109,

111-117, 119, 121, 123-136 are dependent directly or indirectly on claim 107 and therefore incorporate all the limitations thereof. Accordingly, Chen also fails to anticipate these dependent claims.

Similarly, claim 137 is directed to an expression vector encoding two or more different double stranded RNA sequences that are homologous and complementary to two or more sequences of at least one target gene. As explained above, Chen concerns ribozymes and therefore does not teach the expression of double stranded RNA sequences that are homologous and complementary to a target gene. Claims 139, 141-148, 156-157, 159, 163, 165, 167, 168 and 170-173 are dependent directly or indirectly on claim 137 and therefore incorporate all the limitations thereof. Accordingly, Chen also fails to anticipate these dependent claims.

In view of the above remarks, reconsideration and withdrawal of the rejection under §102(b) based on Chen are respectfully requested.

Claims 150-155 were rejected under 35 U.S.C. §102(e) as being anticipated by Taira *et al.* (US 2005/0197315). According to the Office Action, Taira *et al.* teach an expression vector comprising two polIII promoters capable of generating multiple double stranded RNA molecules (with reference to Figures 2, 18 and 25). Applicants respectfully traverse the rejection.

Applicants have reviewed the figures from Taira *et al.* cited in the Office Action as disclosing the claimed invention, and Applicants do not see where these figures teach multiple double stranded RNA molecules expressed from a single

expression vector. Instead, these figures show sense and antisense sequences behind one or more promoters, which anneal following expression to form a single double stranded RNA. Accordingly, the reference does not appear to teach an expression vector capable of generating multiple different double stranded RNAs as recited in the instant claims.

In any case, Applicants respectfully submit that Taira *et al.* is not prior art to instant claims 150-155, because claims 150-155 deserve the benefit of the parent PCT filing date for the reasons discussed above. Reconsideration and withdrawal of the rejection under §102(e) based on Taira *et al.* are respectfully requested.

Claims 107, 117, 119-120, 137, 157, 159-160, 164 and 166 have been rejected under 35 U.S.C. §102(e) as being anticipated by Ruiz *et al.* (US 5,912,149) (hereinafter US '149). According to the Office Action, US '149 teaches a multitarget partially double stranded RNA molecule comprising two different double stranded RNA sequences that are complementary to two sequences of a HBV target gene (with reference to Figure 1A and 1B). Applicants respectfully traverse the rejection.

US '149 concerns a multimeric ribozyme containing multiple repeating units, wherein each unit is a ribozyme containing a catalytic domain and an antisense domain (abstract). At no point does US '149 teach a multitarget partially double stranded RNA molecule comprising two or more different double stranded RNA sequences that are substantially complementary and homologous to two or more sequences of a target gene, as recited in claim 107.

As depicted in Figure 1B of US '149, ribozymes do contain sequences that are complementary to the target gene (*i.e.*, sequences complementary to the target HBV RNA). Further, ribozymes do contain a partially double stranded catalytic segment. However, the double stranded segment in a ribozyme is neither homologous nor complementary to the target gene. Accordingly, US '149 does not anticipate claim 107. Claims 117 and 119-120 are dependent directly or indirectly on claim 107 and therefore incorporate all the limitations thereof. Accordingly, US '149 also fails to anticipate these dependent claims.

Similarly, claim 137 is directed to an expression vector encoding two or more different double stranded RNA sequences that are homologous and complementary to two or more sequences of at least one target gene. As explained above, US '149 concerns ribozymes and therefore does not teach the expression of double stranded RNA sequences that are homologous and complementary to a target gene. Claims 157, 159-160, 164 and 166 are dependent directly or indirectly on claim 137 and therefore incorporate all the limitations thereof. Accordingly, US '149 also fails to anticipate these dependent claims.

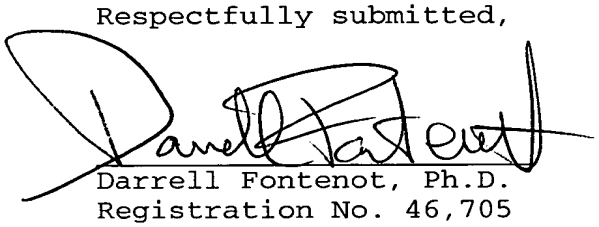
In view of the above remarks, reconsideration and withdrawal of the rejection under §102(b) based on US '149 are respectfully requested.

Conclusion

With this amendment, it is believed the application is now in condition for allowance, because Applicants have satisfied all of the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §§ 112

and 103. It is further requested that Examiner Nguyen reconsider the patentability of rejected claims 107-168 and 170-173 in light of remarks herein provided and withdraw all rejections, thereby placing the application in condition for allowance. A timely Notice of Allowance is therefore solicited. In the event that any issues remain, Examiner Chong is requested to contact the undersigned attorney at 845-602-3144 to resolve them.

Respectfully submitted,



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